Remarks

Claims 1-35 and 48 are pending in this application. Claim 6 has been canceled without prejudice. Claims 7 and 8 have been amended merely to adjust claim dependencies. Claim 1 has been amended to delete certain values for R^4 and to clarify the definition of "substituted phenyl" in the definition of R^3. Claim 21 has been amended to correct a typographical error. Support for the amendments can be found throughout the specification and original claims as originally filed, for example, at page 16, lines 19-25 (definition of "substituted phenyl"); and at page 16, line 32 (R^1 is methyl or ethyl). No new matter has been added. After entry of this amendment, claims 1-5, 7-35, and 48 will be pending in this application.

I. Elections

The Office has required restriction between the following nine Groups:

I. Claims 1-26 and 38-43, drawn to examples 1, 41, and compositions thereof, classifiable in several non-heterocyclic classes (558, 562, etc.), numerous subclasses;

II Claims 1-26 and 38-43, drawn to examples 2-8, 21-28, 50, 53, 55-56, and compositions thereof, classifiable in several non-heterocyclic classes (558, 562, etc.), numerous subclasses;

III. Claims 1-26 and 38-43, drawn to example 9 and composition thereof, classifiable in several non-heterocyclic classes (558, 562, etc.), numerous subclasses;

IV. Claims 1-26 and 38-43, drawn to examples 10-20, 29-32, 34-40, 42-44, 47-49, 51-52, 54, 57, and compositions thereof, classifiable in several non-heterocyclic classes (558, 562, etc.), numerous subclasses;

V. Claims 1-26 and 38-43, drawn to example 33 and composition thereof, classifiable in several non-heterocyclic classes (558, 562, etc.), numerous subclasses;

VI. Claims 1-26 and 38-43, drawn to examples 45-46 and compositions thereof, classifiable in several non-heterocyclic classes (558, 562, etc.), numerous subclasses;

VII. Claims 1-26 and 38-43, drawn to any compound in the claims but not in groups I-VI above and compositions thereof, classifiable in several non-heterocyclic classes (558, 562, etc.), numerous subclasses;

VIII. Claims 27-35, drawn to various methods of using compounds of groups I-VII, classifiable in several non-heterocyclic classes (514, 558, 562, etc.), numerous subclasses; and

IX. Claims 1-26 and 38-43, drawn to a process of making, classifiable in several non-heterocyclic classes (558, 562, etc.), numerous subclasses.

(Restriction Requirement, pages 2-3). Upon election of Group VIII or IX, the Office further requires election of one of Groups I to VII. Upon election of Group VIII, the Office also requires an election of a specific disease. Accordingly, Applicants hereby elect Group VIII (pending claims 27-35) **with traverse**. As Group VIII was elected, Applicants further elect the disease state, dyslipidemia, **with traverse**.

Upon election of any of Groups I to IX, the Office further requires an "election of a single compound (or set of compounds)...including an exact definition of each substitution on the base molecule (Formula I), wherein a single member at each subsitutent group or moiety is selected" (Restriction Requirement, page 3). By stating that Applicants must select a single member at each substituent group, the Office appears to contradict its earlier statement that Applicants can elect a "set of compounds". In the absence of any further clarification, Applicants interpret this statement as requiring an election of a single compound.

As to the identification substituent groups, the Office again contradicts itself as to the required degree of specificity. The Office first appears to indicate that the substituents can be generically defined (e.g., aryl) by stating:

> For example, if a base molecule has a substituent group R1, wherein R1 is recited to be any one of H, OH, COOH, aryl, alkoxy, halogen, amino, etc., then applicant must select a single subsitutent of R1, for example OH or **aryl**, and each subsequent variable position.

(Restriction Requirement, pages 3-4, *sic*, emphasis added). After implying that the substituents may be generically defined, the Office proceeds to state that the "elected subsitutents must be specific not generic so as to define a species" (Restriction Requirement, page 4). In the absence of any further clarification, Applicants have identified the substituent groups specifically.

As Group VIII was elected, Applicants further elect **with traverse** Group II and compound 28, 5-methyl-4-oxo-5-thiophen-3-yl-4,5-dihydro-furan-2-carboxylic acid, wherein R^1

is H, R^2 is H, R^3 is thien-3-yl and R^4 is methyl. Claims 1, 4-7, 11-13, 15, 17, 19-20, 22, 25-35, and 48 read on compound 28. In particular, claims 27-35 of Group VIII read on compound 28.

II. Traversal of the Restriction Requirement

As a threshold matter, it is clear that this restriction requirement has not been perfected as the metes and bounds of the restricted groups suffer from ambiguity and potential voids in the claimed subject matter. In order to be fully responsive, Applicants have traversed the restriction requirement as summarized herein. However, Applicants respectfully urge the Office to address the ambiguities discussed herein and reissue the restriction requirement so that Applicants can more completely assess and then address the issues surrounding the restriction and election of species requirements.

Applicants respectfully assert that the restriction requirement is improper, because: (A) the restriction requirement arbitrarily fragments claim 1, thereby depriving Applicants of the right to have each claim examined on the merits, raising the spectre of a lack of written description for the subgenera, unfairly denying Applicants the protection of 35 U.S.C. § 121 for a later-filed divisional application, and prospectively withdrawing subject matter from examination from the present and subsequent applications; B) the claims have unity of invention; and (C) the restriction requirement involves arbitrary groupings.

(A) Arbitrary fragmentation and lack of clarity

The restriction requirement arbitrarily fragments claim 1 into seven artificial subgeneric groups, thereby depriving Applicants of their right to have each claim examined on the merits, raising the spectre of a lack of written description for the subgenera, unfairly denying Applicants the protection of 35 U.S.C. § 121 for a later-filed divisional application, and prospectively withdrawing subject matter from examination from the present and subsequent applications. As will be appreciated, an applicant has a right to have each claim examined on the merits. *In re Weber*, 198 U.S.P.Q. 328, 331 (C.C.P.A. 1978). Restriction of a single Markush claim into several subgenera, however, may deprive an applicant of this right. In *Weber*, the CCPA cautioned that:

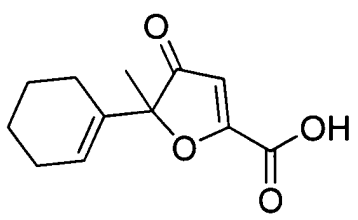
> If an applicant submits a number of claims, it may well be that pursuant to a proper restriction requirement, those claims will be dispersed to a number of applications. Such action would not affect the right of the applicant eventually to have each of the claims examined in the form he considers to best define his invention. If, however, a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits. The totality of the resulting fragmentary claims would not necessarily be the equivalent of the original claim. Further, since the subgenera would be defined by the examiner rather than by the applicant, it is not inconceivable that a number of the fragments would not be described in the specification.

198 U.S.P.Q. at 331. Hence, when the Office fragments a single Markush claim into several groups, the definition of those groups may result in the totality of the resulting fragmentary claims not being equivalent to the original claim, for example, by introducing voids and ambiguities. *Id.* Such voids may improperly withdraw claimed subject matter permanently from consideration not only in the pending application, but also prospectively in any subsequent application. *See In re Haas*, 179 U.S.P.Q. 623, 625 (C.C.P.A. 1973) (holding that an Examiner's withdrawal of claims under 35 U.S.C. 101 and 121 as being multiple patentable distinct inventions amounted to a rejection and an improper withdrawal of the claims from consideration in any subsequent application). Further, the Office may define the subgeneric groups completely apart from the written description embraced by the dependent claims and the specification, such that one or more of the groups lack written description support. *Id.* (citing *Fields v. Conover*, 170 U.S.P.Q. 276 (C.C.P.A. 1971), wherein a subgenus was not described by a genus, and *In re Ruschig*, 154 U.S.P.Q. 118 (C.C.P.A. 1967), wherein a species was not described by a genus).

Additionally, the Office's fragmentation of a Markush claim may lead to a lack of clarity, thereby unfairly subjecting an applicant to an obviousness-type double patenting rejection of a later-filed divisional application. As will be appreciated, the Office is required to "provide a clear and detailed record of the restriction requirement to provide a clear demarcation between restricted inventions so that it can be determined whether inventions claimed in a continuing application are consonant with the restriction requirement and therefore subject to the prohibition against double patenting rejections under 35 U.S.C. § 121." M.P.E.P. § 814, citing *Geneva*

Pharmaceuticals. Inc. v. GlaxoSmithKline PLC, 349 F.3d 1373, 1381 (Fed. Cir. 2003). These consequences deprive the applicant of the right to have the single claim examined on its merits.

As currently formulated, the Office's restriction of claim 1 into seven subgeneric groups (Groups I to VII) deprives Applicants' of the right to have their right to have claim 1 examined on its merits. First, the Office has defined the Groups in an ambiguous manner such that the restriction requirement fails to provide a clear line of demarcation between the restricted inventions. In particular, the Office defines Groups I to VI as being drawn to particular examples of claim 1 and compositions thereof. For example, Group I is "drawn to examples 1, 41, and composition thereof" (see structures of examples 1 and 41 below). Other than referring to these two examples, the definition of the Group I does not specify the values for R^1, R^2, R^3, and R^4, thereby rendering the scope of the Group I unclear. For example, it is unclear whether each substituent of Group I is specifically (e.g., R^3 is cyclohexenyl) or generically defined (e.g., R^3 is C_{3-7} cycloalkenyl). Further, it is unclear whether the Group I is being restricted according to the definitions of every variable in the listed examples (e.g., R^3 is C_{3-7} cycloalkenyl, R^4 is methyl, etc.) or whether it is being restricted according to only one substituent in the listed examples (e.g., R^3 is C_{3-7} cycloalkenyl, while R^2, R^3, and R^4 may have any of the values recited in claim 1). Groups VII to IX also lack clarity due to the ambiguities in Groups I-VI. Group VII is drawn to any compound in the claims but not in groups I to VI, and compositions thereof. Because Groups I to VI are not clearly defined in the restriction requirement, the exact line of demarcation between Group VII and the other groups is unclear. Further, as the Office has required an election of one of Groups I to VII upon election of Group VIII or IX, the lack of clarity in the definitions of Groups I to VII also renders the scope of Groups VIII and IX unclear.



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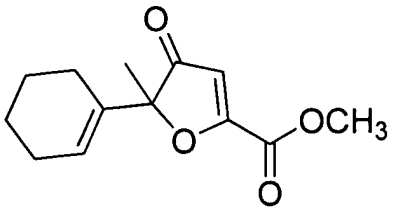


(41)

By introducing these ambiguities, the Office has failed to properly provide a clear and detailed record of the restriction requirement as required by M.P.E.P. § 814 and the decision in

Geneva Pharmaceuticals. This can potentially deprive Applicants the protection of 35 U.S.C. § 121 for a later-filed divisional application, by blurring the line of demarcation between the restricted Groups.

Further, as discussed previously, the fragmentation of a Markush claim can lead to potential problems with written description. Applicants are unable to evaluate the existence or magnitude of any such problem with Groups I to VII, because of the ambiguous definitions of Groups I to VII. For example, Group VII is defined as "any compound in the claims but not in groups I-VI" with the further provision that the "compound must be disclosed in the specification" (Restriction Requirement, page 2). While Applicants suspect this catch-all definition may not be supported by the specification, the exact scope of Group VII is impossible to assess because of the lack of clarity surrounding the definitions of Groups I to VI. If a Group does not have written description support, Applicants would be forced to divide and reformulate the subject matter of each Group into multiple claims according to the support of the specification and claims. The scope of the resulting fragments of these multiple claims would not equal the original scope of claim 1, being marred with voids and ambiguities. Accordingly, Applicants would have no choice but to forego rights to subject matter to which they are entitled. Forced forefeiture of rights resulting from the contrived and artificial delineation of the compound/composition claims into Groups I to VII for mere administrative convenience is clearly beyond the bounds of statutory authority. *Weber*, 198 U.S.P.Q. at 332 (concluding that statutory rights are paramount to administrative convenience such as control of examiner caseloads and the amount of searching per application).

For the above reasons, it is clear that the outstanding restriction requirement is seriously flawed. Applicants respectfully request that the restriction requirement be withdrawn or, at a minimum, that Groups I to VII be rejoined as a single group.

(B) Unity of invention

The Office states that unity is lacking because the inventions of Groups I to IX allegedly do not share a special technical feature under PCT Rule 13. As will be appreciated, "unity of invention (not restriction) practice is applicable in ... national stage applications submitted under 35 U.S.C. 371." M.P.E.P. § 1893.03(d). Unity of invention must be determined under the

provisions of the PCT in a national stage application filed under 35 U.S.C. § 371. *Caterpillar Tractor Co. v. Com'r Pat. & Trademarks*, 650 F. Supp. 218 (E.D. Va. 1986). The legal standard for determining unity of invention is set forth in Rule 13, which states, in part:

> the requirement of unity of invention ... shall be fulfilled ... when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

P.C.T. Rule 13.2; M.P.E.P. § 1850. The presence of a special technical feature linking the claims thus defines the unity of invention standard.

Annex B to the Administrative Instructions under the P.C.T. (the "Administrative Instructions") and in Chapter 10 of the P.C.T. International Search and Preliminary Examination Guidelines, and M.P.E.P. § 1850 set forth guidelines for determining unity of invention for Markush claim. In particular, when a series of chemical compounds is defined in a claim using so-called "Markush practice" enumerating alternative elements, "[t]he fact that the alternatives of a Markush grouping can be differently classified shall not, taken alone, be considered to be justification for a finding of a lack of unity of invention." M.P.E.P. § 1850. Instead, unity of invention will be established if:

> (A) All alternatives have a common property or activity; and
>
> (B) (1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or
>
> (B) (2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

M.P.E.P. § 1850. The term "significant structural element...shared by all of the alternatives" refers to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. M.P.E.P. § 1850.

(i) Groups I to VII

The Office alleges that the only structural element shared by Groups I to IX is the 4-oxo-4,5-dihydro-furan-2-carboxylate moiety. (Restriction Requirement, page 3). The Office, however, asserts that this moiety is obvious and/or not novel, citing to D2-D4 of the International Search Report (ISR) for PCT/US2004/038920. Hence, the Office concludes that the 4-oxo-4,5-dihydro-furan-2-carboxylate moiety does not constitute a special technical feature linking the claims (Restriction Requirement, page 3). Applicants respectfully disagree.

The Office has not established that the common features of the compounds in claim 1, as amended, do not constitute a significant technical feature linking the claims. The compounds according to claim 1 in fact have other common features, beyond the 4-oxo-4,5-dihydro-furan-2-carboxylate moiety. For example, common features include:

- a 4-oxo-4,5-dihydro-furan-2-carboxylate moiety
- substitution by a **cyclic** R^3 group
- the carboxylate group and the cyclic R^3 group are in a fixed 2,5-relationship to each other

Additionally, Applicants have submitted amendments to claim 1, which reduce the number of points of variability in the R^3 and R^4 substituents attached at the 5-position. As to the Office's *a posteriori* determination of lack of unity based on D2-D3 of the ISR for PCT/US2004/038920, the Office's analysis did not take into account the claim amendments submitted herein and, therefore, cannot form a basis for the alleged lack of unity of invention for the amended claims. Thus, Applicants respectfully submit that the Markush group recited in claim 1 (and in Groups I to VII), as currently amended, embraces chemical compound alternatives that share a significant structural element, and as such, at least meets prong (B)(1) of the PCT unity of invention criteria for Markush practice.

Further, the compounds of Groups I to VII share the common utilities of modulating the RUP25 receptor and treating metabolic related disorders. Hence, the Markush group recited in

claim 1, as currently amended, meets prong (A) of the PCT unity invention criteria for Markush practice. As the compounds of Groups I to VII meet both prongs of the test for unity of invention and for the reasons summarized herein, Applicants respectfully request reconsideration and withdrawal of the restriction requirement. Alternatively, as Applicants have elected Group VIII and have further elected Group II, Applicants respectfully request that the Office examine the methods of Group VIII with respect to the compounds and compositions of each of Groups I to VII for the reason summarized herein.

(ii) Rejoinder of Groups VIII and IX with Groups I to VII

The restriction requirement is improper as requiring restriction among claims to compounds and compositions (in Groups I-VII), methods of using these compounds (in Group VIII), and processes of making these compounds (in Group IX). M.P.E.P. § 1850 provides that:

> The method for determining unity of invention under PCT Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application:
>
> (A) In addition to an **independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product**...
>
> ...a process shall be considered to be specially adapted for the manufacture of a product if the claimed process inherently results in the claimed product with the technical relationship being present between the claimed product and claimed process. The words "specially adapted" are not intended to imply that the product could not also be manufactured by a different process.

Since the claims in Group VIII relate to a use of the compounds and compositions recited in Groups I to VII, the claims of Group VIII have unity of invention with Groups I to VII under 37 C.F.R. § 1.475(b)(2). Further, as "admixing a compound according to claim 1 and a pharmaceutically acceptable carrier", as recited in claim 1, will inherently produce the claimed compositions of Groups I to VII, the claim of Group IX has unity of invention with Groups I to VII. As Applicants have elected Group VIII and have further elected Group II, Applicants

request rejoinder of Group VIII and IX with Groups I to VII (section II.B.i) for the reasons summarized in this response.

(C) Arbitrary Groupings

Even if unity of invention is found to be lacking as to one or more claims, the Office is not thereby given "carte blanche" under the PCT to divide Applicants' claims as he sees fit because Applicants have the "right to include in a single application ... those inventions which are so linked as to form a single general inventive concept", M.P.E.P. § 1893.03(d). Therefore even if there is lack of unity of invention as to some of the claims, restriction is permissible only to the extent necessary to restore unity of invention. The Applicants are entitled to retain in the application all of the subject matter sharing unity of invention with the Applicants' elected Group.

Focusing on the Applicants' elected Group, even if the Office had been successful in showing lack of unity of invention, the Office does not explain why Groups I to VII should be limited to specific examples disclosed in the specification (and compositions thereof) or, indeed, why each Group was constituted as described in the restriction requirement (see also section II.A below for the lack of clarity in the restriction requirement). There is also no basis for the Office to require restriction between the method of use or process of making claims and the compound and composition claims, since claims to a product, method of its use, and a process specially adapted to the manufacture of a process, share unity of invention under proper PCT practice described above. Hence, Applicants respectfully request reconsideration and withdrawal of the restriction requirement or, at a minimum, rejoinder according to the suggestions in section II.B.

As a final note, Applicants respectfully note that the search can be accomplished without undue burden on the Examiner. In fact, the corresponding PCT application (PCT/US2004/038920) with similar chemical claim scope was searched by the EPO search authority. Further, there are various additional reasons why the claims of Groups I to IX may be searched together without undue burden on the Examiner. Groups I to VII share a common core moiety, 4-oxo-4,5-dihydro-furan-2-carboxylate. Current structure searching techniques readily

allow this core moiety to be searched as a single query with optional substitution at any position. In addition, R^3 at the 5-position of the core moiety may be restricted to a cyclic moiety further simplifying the search parameters. Further, the single search for compounds of Groups I to VII having the core moiety above will inevitably uncover references related to methods of using and processes of making these compounds. For these reasons, there would be no undue burden for the Examiner to search and examine the claims of all of the Groups together.

III. Traversal of the Election of Species Requirements

As a preliminary matter, Applicants note that the Office has required an election of a compound species if one of Groups I to IX is elected and the election of a disease state if Group VIII or IX is elected. Applicants further note that the Office has not clarified whether these two election of species requirements are provisional election of species requirements. If these requirements are provisional in nature, Applicants respectfully urge the Office to reissue the restriction requirement clarifying the nature of the election of species requirements. If this election of species requirement is not provisional in nature, Applicants respectfully note that the Office has failed to give any reason why each compound species within each of Groups I to VII, or each disease state within Group VII, lacks unity of invention with every other species within that group. As will be appreciated, the Office is required to explain why each restricted group (or species) lacks unity with each other group (or species). M.P.E.P. § 1893.03(d).

Additionally, when the members of a Markush group are "so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they may be directed to independent and distinct inventions." M.P.E.P § 803.02. In such a case, it is inappropriate for the examiner to require a provisional election of a single species. M.P.E.P § 803.02. For the reasons summarized above, Applicants respectfully assert that a search for each of the suggested rejoined Groups, can be conducted without serious burden on the Office. Accordingly, Applicants respectfully request that the requirement for an election of species be withdrawn.

Further, Applicants respectfully assert that each disease state encompassed by claims 27-35 may be searched without undue burden. Current key word searching techniques readily allow separate key words, such as the names of the disease states recited by the claims, to be searched in a single query. Accordingly, a search of each of the disorders of Group VIII should involve only a single query and, thus, does not constitute a serious burden on the Examiner. Applicants, therefore, respectfully request withdrawal of the election of species requirement for Group VIII.

IV. Conclusion

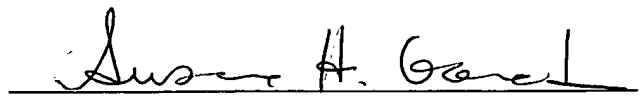
In summary, it is clear that this restriction and election of species requirement has not been perfected as the metes and bounds of the restricted groups suffer from ambiguity and potential voids in the claimed subject matter. In order to be fully responsive, Applicants have traversed the restriction requirement as summarized herein. However, Applicants respectfully urge the Office to address the ambiguities discussed herein and reissue the restriction requirement so that Applicants can more completely assess and then address the issues surrounding the restriction and election of species requirements.

Applicants respectfully request reconsideration of the requirement for restriction and election and rejoinder of the Groups in light of the above comments. Further, early reconsideration and allowance of all pending claims is respectfully requested.

The Commissioner is hereby authorized to debit any fee due or credit any overpayment to Deposit Account No. 06-1050. Further, if not accompanied by an independent petition, this paper constitutes a Petition for an Extension of Time for an amount of time sufficient to extend the deadline and authorizes the Commissioner to debit the petition fee and any other fees or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: March 26, 2008



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